



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

APR 22 2005

Dr. Armand Lione, President
Associated Pharmacologists
& Toxicologists
533 Fourth Street, SE
Washington, D.C. 20003-4222

Docket No. 1983P-0187/CP3

Dear Dr. Lione:

This letter responds to your citizen petition dated April 24, 2000, asking the Food and Drug Administration (FDA) to withdraw approval of the Today Contraceptive Sponge (the Sponge). Your petition states that the Sponge cannot be used as recommended without frequently causing damage to genital tissues that increases the risk of toxic shock syndrome (TSS) and infection with the Human Immunodeficiency Virus (HIV). For the reasons that follow, your petition is denied.

I. Background

The Sponge is a nonprescription contraceptive drug product designed for use by women. It consists of a round piece of polyurethane foam and a spermicide. The active ingredient in the Sponge is nonoxynol 9 (N-9), a commonly used spermicide that has been available over the counter (OTC) for over 30 years (45 FR 82014 at 82029; December 12, 1980). FDA required the Sponge to be the subject of an approved new drug application (NDA) before marketing. In April 1983, FDA approved VLI Corporation's NDA 18-683 for the Sponge. In 1987, the NDA was transferred to Whitehall-Robins. Whitehall-Robins voluntarily ceased production of the Sponge in August 1993 because of manufacturing problems and withdrew the Sponge from the market in January 1995. In March 1999, the NDA was transferred to Allendale Pharmaceuticals. Allendale Pharmaceuticals submitted a manufacturing supplement in March 2004. After a thorough review of the manufacturing processes, the product labeling, and the safety concerns described in your petition, FDA today approved Allendale Pharmaceuticals' supplement to market the Sponge.

II. The Applicable Legal Standard

The Federal Food, Drug, and Cosmetic Act provides that FDA shall withdraw approval of an application:

... if the Secretary finds (1) that clinical or other experience, tests, or other scientific data show that such drug is unsafe for use under the conditions of use upon the basis of which the application was approved; [or] (2) that new evidence of clinical experience, not contained in such application or not available to the Secretary until after such application was approved, or tests by new methods, or

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tests by methods not deemed reasonably applicable when such application was approved, evaluated together with the evidence available to the Secretary when the application was approved, shows that such drug is not shown to be safe for use under the conditions of use upon the basis of which the application was approved (21 U.S.C. 355(e)).

Thus, to justify your request that the Agency withdraw approval of the Sponge, you would need to provide information to demonstrate (1) that the Sponge is unsafe for use under the conditions for which it was approved, or (2) that the Sponge is not shown to be safe. For the reasons discussed below, you have not provided evidence to justify withdrawal of the Sponge. Furthermore, we have considered the available evidence (not just that contained in your petition) and do not believe the evidence supports withdrawal of the Sponge's approval.

III. The Petition's Claims and FDA's Responses

A. Harmful Alterations in the Vaginal Environment Caused by N-9

You state that research shows that "in adequate doses and with frequent use, N-9 alters the vaginal flora to increase the likelihood that pathogens will survive" (Petition at 3). You cite in vitro studies by Ongradi,¹ Klebanoff,² McGroarty,³ and O'Connor,⁴ and clinical studies by Rosenstein⁵ and Stafford⁶ to support your assertion concerning N-9 and the survival of pathogens (Petition at 3-4). We agree that use of N-9 alters the vaginal flora but do not agree that the temporary alteration in flora creates a clinical problem.

Normally, the microbial flora of the vagina is lactobacilli, including some hydrogen peroxide-producing strains. These lactobacilli help to maintain the vagina's acidic pH and prevent the overgrowth of other types of bacteria. At times, the vagina can become colonized with other types of bacteria like enteric bacteria from the bowel (*Escherichia coli*, *enterococcus*) or the bacteria that cause bacterial vaginosis. Bacterial vaginosis is a clinical syndrome where several

¹ Ongradi, J., et al., "Acid Sensitivity of Cell-Free and Cell-Associated HIV-1. Clinical Implications," *AIDS Research and Human Retrovirus*, 6:1433-1436, 1990.

² Klebanoff, S.J. and R.W. Coombs, "Virucidal Effect of *Lactobacillus Acidophilus* on Human Immunodeficiency Virus Types: Possible Role of Heterosexual Transmission," *The Journal of Experimental Medicine*, 174:289-292, 1991

³ McGroarty, et al., "Influence of Spermicidal Compound Nonoxynol-9 on the Growth and Adhesion of Urogenital Bacteria In Vitro," *Current Microbiology*, 21:219-223, 1990.

⁴ O'Connor, et al., "The Activity of Candidate Virucidal Agents, Low pH and Genital Secretions Against HIV 1 *In Vitro*," *International Journal of STD & AIDS*, 6:267-272, 1995.

⁵ Rosenstein, et al., "Effect on Normal Vaginal Flora of Three Intravaginal Microbicidal Agents Potentially Active against Human Immunodeficiency Virus Type 1," *The Journal of Infectious Diseases*, 177:1386-1390, 1998.

⁶ Stafford, et al., "Safety Study of Nonoxynol-9 as a Vaginal Microbicide: Evidence of Adverse Effects," *Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology*, 17:327-331, 1998.

species of vaginal bacteria replace the normal lactobacilli and may cause vulvovaginitis symptoms. The bacteria associated with bacterial vaginosis include *Gardnerella vaginalis*, *Mycoplasma hominis*, and various Gram negative and Gram positive anaerobes. Bacterial vaginosis is a sexually associated condition but is not a specific sexually transmitted infection. Only patients with symptoms require treatment, and treatment is not recommended for asymptomatic carriers or male partners. The most common symptom is excessive or malodorous vaginal discharge, but women may also experience erythema, edema, and itching of the external genitalia.⁷ Many factors contribute to alterations in normal vaginal flora including: naturally occurring changes in hormone levels, antibiotic use, tampon use, use of an intrauterine device, diaphragm use, spermicide use, douching, a history of sexually transmitted infections, and sexual contact.

The Ongradi, Klebanoff, McGroarty, and O'Connor studies were in vitro studies, not clinical studies. These studies merely suggest a theoretical mechanism by which N-9 can alter the normal flora of the vagina. The Stafford and Rosenstein publications submitted by the petitioner report clinical data from the same group of study subjects and represent only one clinical study. Stafford and Rosenstein author both publications.

The 1998 randomized, placebo-controlled study by Stafford and Rosenstein evaluated the use of a 100 milligram (mg) N-9 gel or a placebo gel for 7 consecutive days in 40 women. During the study, women did not have sexual intercourse and did not use other intravaginal products. All 40 women completed the study. Transient decreases in lactobacilli were seen in 56 percent of women using the N-9 gel and in 33 percent of women using the placebo gel. In all cases, lactobacilli were regained by the seventh day after gel exposure stopped. A detailed microbiologic investigation was completed on a subgroup of 16 women in the N-9 group and 18 women in the placebo group.⁸ This analysis yielded the following results.

- Abnormal vaginal flora were present with or without depletion of lactobacilli and were characterized by large numbers (10^5 colony forming units) of Gram positive and Gram negative aerobic bacteria including: staphylococcus species, micrococcus species, *Eschericia coli* (*E. coli*), *Klebsiella pneumonia*, and *Enterobacter aerogenes*.
- After seven days of gel use, none (0%) of the women in the N-9 group and nine (69%) of the women in the placebo group had normal vaginal flora. This was a statistically significant difference ($p < 0.0005$).
- One week later, eight (67%) of the women in the N-9 group and nine (69%) of the women in the placebo group had normal vaginal flora.
- The presence or absence of hydrogen peroxide-producing strains of lactobacilli did not influence the incidence of colonization with other bacteria or the recovery of normal flora.

⁷ Cates, W., "Reproductive Tract Infections." *Contraceptive Technology* 18th edition. 202, 2004.

⁸ Analysis was performed only on the women with normal vaginal flora at the beginning of the study (12 in the N-9 group and 13 in the placebo group).

Rosenstein concluded that the changes in vaginal flora seen in the N-9 study did not predispose the women to bacterial vaginosis, which is usually characterized by an overgrowth of anaerobic bacterial species. Women who maintained a normal population of lactobacilli were more likely to recover normal vaginal flora by seven days after completing gel use.

The Stafford and Rosenstein study and other published studies⁹ suggest that intravaginal N-9 may temporarily decrease or eliminate some strains of lactobacilli in the vagina and allow vaginal colonization with other bacteria. We do not believe that these transient changes in vaginal flora warrant withdrawal of the Sponge approval. The current label for the Sponge warns of possible vaginal irritation. If symptoms were to occur as a result of bacterial vaginosis, users of the product are alerted to stop use and talk to a doctor.

B. N-9 Irritation and Erosions of the Vaginal Epithelium

Data from trials studying N-9 formulations other than the Sponge demonstrate that frequent N-9 use (more than once a day) may lead to vaginal irritation and in some instances may involve epithelial breach or disruption (abrasions, ulcerations). On January 16, 2003, FDA published a proposed rule for Over-the-Counter Vaginal Contraceptive Drug Products Containing Nonoxynol-9; Required Labeling (the N-9 proposed rule) that reviews the scientific literature on vaginal irritation associated with N-9 use (68 FR 2254 at 2255 to 2258). A copy of the proposed rule is enclosed. The literature suggests that infrequent use of N-9 products (once a day or less) does not result in an increased rate of epithelial disruption.

You state that the rates of irritation and tissue damage associated with the Sponge are higher than the rates associated with the use of other N-9 containing contraceptives (Petition at 9). You have not presented evidence to support your assertion that the rates are higher with the Sponge. There are only two published studies that have looked specifically at vaginal and cervical irritation and ulceration associated with use of the Sponge. These studies are discussed below.

A study by Poindexter¹⁰ compared the incidence of vulvar, vaginal, and cervical abnormalities following seven days of N-9 use in three formulations: the Sponge, Conceptrol gel (a cellulose-based gel containing 0.1 gram (g) of N-9), and Advantage 24 gel (a polycarbophil-based gel containing 0.05 g of N-9). Conceptrol and Advantage-S (new name for Advantage 24) are currently marketed in the United States. The Poindexter study was a crossover study where each subject used each of the three products during different treatment periods. Despite a washout period of 21 days or more and the requirement for normal colposcopy before beginning the next treatment, the data demonstrated a treatment period effect for abnormalities seen after use of the

⁹ Watts, D.H., L. Rabe, and M.A. Krohn, "The Effects of Three Nonoxynol-9 Preparations on Vaginal Flora and Epithelium," *Journal of Infectious Diseases*, 180:426-437, 1999. Gupta, K., S. L. Hillier, and T.M. Hooton, "Effects of Contraceptive Method on the Vaginal Microbial Flora: A Prospective Evaluation," *Journal of Infectious Diseases*, 181:595-601, 2000. Richardson, B.A., H.L. Martin, and C.E. Stevens, "Use of Nonoxynol-9 and Changes in Vaginal Lactobacilli," *Journal of Infectious Diseases*, 178:441-445, 1998.

¹⁰ Poindexter, et al., "Comparison of Spermicides on Vulvar, Vaginal, and Cervical Mucosa," *Contraception*, 53:147-153, 1996.

Advantage product. Consequently, a valid comparison between Advantage-S (Advantage 24) and the Sponge cannot be made. A valid comparison can be made between the Sponge and Conceptrol gel. Each subject was evaluated by visual examination, colposcopy, and Pap smear. The following conditions were assessed and scored on a ten point scale: redness, petechiae, ulceration, infection, punctation, mosaicism, leukoplakia, nonstaining squamous epithelium, and white epithelium. Abnormalities of the vulva, vagina, and cervix occurred less often following 7 days of Sponge use, compared with 7 days of Conceptrol gel use. These results were statistically significant for findings on colposcopy and Pap smear. Contrary to the petitioner's assertion, the Poindexter study suggests that the Sponge is not more irritating and is possibly less irritating than a contraceptive N-9 gel marketed under the OTC monograph.

Kreiss¹¹ studied 138 sero-negative sex workers in Nairobi and randomized 74 women to the N-9 Sponge and 64 to a comparator suppository or cream that did not contain N-9. The women in the study used the Sponge an average of 14 times per week for more than 1 year. Women using the N-9 Sponge had a higher rate of conversion from HIV negative to HIV positive. A total of 21 women (43%) of the N-9 group and 19 women (35%) of the placebo group converted from HIV negative to HIV positive. Women in the N-9 Sponge group had an increased incidence of genital ulcerations compared to the comparator group. However, the results were confounded by a significantly higher rate of genital ulcers in the N-9 group at the time of enrollment. This discrepancy may indicate a randomization flaw in the study design and raises questions about the significance of this finding. The authors hypothesized that N-9 use would reduce the risk of HIV seroconversion. When study results indicated that there was no decrease, and perhaps an increase, in HIV seroconversion, the study hypothesis was rejected and the study was discontinued.

You also dispute a statement made by the sponsor in the labeling of the product that only 125 mg of N-9 are released from the Sponge during each use and argue that the claim of a single number, rather than a range, is suspect because the Sponge contains a reservoir of 1,000 mg of N-9 (Petition at 6). The current Sponge label lists the amount of N-9 in the product as 1000 mg. During the initial NDA review, FDA had access to information on the amount of N-9 eluted from the Sponge during use. Investigators analyzed 54 used sponges to determine the amount of N-9 eluted during use. The sponges were worn for up to 48 hours, with a maximum of three coital episodes per Sponge. The investigators found that the range of N-9 released during use was 6 to 503 mg with a mean of 125 mg. Repeated calculations based on original data submitted to the NDA revealed a mean N-9 release of 177.3 mg and a median release of 129 mg. The 129 mg median release of N-9 from the Sponge is comparable in dose to a single use of 100 mg or 150 mg Conceptrol N-9 gel. Twelve of the 54 Sponges eluted 300 to 500 mg of N-9 during up to 48 hours of use. This amount is equivalent to using two to five doses of other OTC spermicide products in a 48-hour period, which is currently permitted under the OTC vaginal contraceptive drug products rulemaking. FDA's proposed rule on "Vaginal Contraceptive Drug Products for Over-the-Counter Human Use" (60 FR 6892; February 3, 1995) does not propose to limit the number of times an OTC spermicide product can be used in a 24- or 48-hour period. The

¹¹ Kreiss, et al., "Efficacy of Nonoxynol-9 Contraceptive Sponge Use in Preventing Heterosexual Acquisition of HIV in Nairobi Prostitutes," *JAMA*, 268: 477-482, 1992.

Poindexter study discussed earlier suggests that use of the Sponge for 7 consecutive days causes no more, and possibly less, irritation of the vagina and cervix than other N-9 preparations. Thus, you have not demonstrated that Sponge users are exposed to a greater amount of N-9 than users of other OTC spermicidal products, and it does not follow that the Sponge causes more irritation and tissue damage than other N-9 containing OTC contraceptives because it contains more N-9.

The results of the studies examining the use of products containing N-9 and genital irritation suggest that increasing frequency of N-9 use leads to an increased incidence of irritation and sometimes to vaginal and cervical lesions involving an epithelial breach.¹² However, there is no convincing evidence that Sponge use is associated with a higher incidence of these events than use of other N-9 formulations. It is unclear how much epithelial disruption or vaginal inflammation should be considered *normal*. In studies where sexual intercourse is allowed, it is difficult to tell whether epithelial changes resulted from sexual intercourse or from use of the N-9 product.

C. Increased Risk of HIV Transmission

You state that the tissue damage caused by the Sponge can increase the risk of HIV transmission (Petition at 1, 5, 8).

FDA agrees that frequent use of products containing N-9 has the potential to increase the risk of HIV transmission in a population at risk for contracting HIV. One randomized, controlled study¹³ conducted in women at high risk of HIV showed that using a 52.5-mg N-9 gel more than three times a day was associated with an increased risk of HIV transmission. The authors hypothesized that this increased risk was related to the detergent-like effects of N-9 and that the resultant vaginal and cervical irritation could disrupt or weaken the epithelial barrier. On May 10, 2002, the Centers for Disease Control and Prevention (CDC) published a report¹⁴ warning women that N-9 contraceptives do not protect against HIV and other sexually transmitted diseases (STDs). On June 28, 2002, the World Health Organization (WHO) issued revised public health guidelines¹⁵ for the use of N-9 for HIV and STD prevention and for pregnancy prevention in populations at high risk for HIV. The WHO guidelines advised that "spermicides containing N-9 do not protect against HIV infection and may even increase the risk of HIV infection in women using these products frequently." The guidelines advise women at high risk of HIV infection to avoid using N-9 spermicides for contraception.

¹² World Health Organization/CONRAD Technical Consultation on Nonoxynol-9. Summary Report, Geneva, October 9-10, 2001, in *Reproductive Health Matters*, 20:175-181, 2002; N-9 proposed rule, 68 FR 2254 at 2255 to 2258; January 16, 2003.

¹³ Van Damme, L. et al., "Effectiveness of COL-1492, a Nonoxynol-9 Vaginal Gel, on HIV-1 Transmission in Female Sex Workers: a Randomized Controlled Trial," *Lancet*, 360: 971-977, 2002.

¹⁴ Centers for Disease Control and Prevention Guidelines System, "Nonoxynol-9 Spermicide Contraception Use—United States, 1999," *Morbidity and Mortality Weekly Report*, 51:389-392, 2002.

¹⁵ WHO Press Release WHO/55, "Nonoxynol-9 Ineffective in Preventing HIV Infection." June 2002.

On January 16, 2003, in response to concerns about N-9 use and the risk of HIV transmission, FDA published the N-9 proposed rule that would require new label statements for all OTC vaginal contraceptive drug products containing N-9 (68 FR 2254 at 2259). These statements would advise consumers that vaginal contraceptives containing N-9 do not protect against infection from HIV or other STDs. The label would also advise consumers that frequent use of vaginal contraceptives containing N-9 can increase vaginal irritation and that this increased irritation may increase the possibility of transmission of HIV and other STDs from infected partners.

Although the proposed rule has not been finalized, FDA has asked the manufacturer of the Sponge to add warnings concerning HIV transmission to the labeling of the Sponge when it is reintroduced to the market. We believe that these warnings adequately inform consumers of the potential increased risk of HIV-transmission associated with use of the Sponge. The specific Sponge warnings concerning HIV are set out below.¹⁶

The outer carton of the Sponge, as approved for reintroduction to the market, contains the following warning and label statements:

Sexually transmitted diseases (STDs) alert: This product does **not** protect against the AIDS virus (HIV) or other STDs.

Ask a doctor before use if you have a new partner, multiple sex partners, or unprotected sex. Frequent use (more than once a day) can increase vaginal irritation, which may increase the risk of getting the AIDS virus (HIV) or other STDs from infected partners.

Stop use and ask a doctor if you or your partner get burning, itching, a rash, or other irritation of the vagina or penis.

Correct use of a latex condom by your partner with every sexual act will help reduce the risk of transmission of the AIDS virus (HIV) and many STDs.

Do not leave Sponge in vagina for longer than 30 hours.

There is a consumer information leaflet inside the carton that contains the following additional information relating to the risk of HIV transmission:

Studies have raised safety concerns that frequent use (more than once a day) of products containing nonoxynol 9 can increase vaginal irritation, which may increase the risk of getting the AIDS virus (HIV) or other STDs from infected partners. Vaginal irritation may include symptoms such as burning, itching, or a rash, or you may not notice any symptoms at all. If you use these products frequently and/or have a new sex partner, or unprotected sex, see a doctor or other health professional for your best birth control and methods to prevent STDs.

¹⁶ When FDA issues a final rule for warning statements on OTC contraceptive drug products containing N-9, the manufacturer of the Sponge will be required to comply with the new regulation.

Correct use of a latex condom with every sexual act will help reduce the risk of getting the AIDS virus (HIV) and other STDs from infected partners.

In sum, FDA has concluded that the Sponge as labeled for reintroduction into the market appropriately warns users of the potential for increased risk of HIV-transmission associated with use of the product with an infected partner. Accordingly, we have also concluded that your arguments concerning an increased risk of HIV transmission do not provide a basis to withdraw approval of the Sponge.

D. Increased Risk of TSS

You assert that by damaging the vaginal and cervical epithelium, the Sponge can increase the risk of TSS, and you request that approval of the Sponge be withdrawn on this ground (Petition at 1). You previously submitted two citizen petitions asking that approval of the Sponge be withdrawn because of risk of TSS.¹⁷

In our August 28, 1997, response to your previous petitions, we concluded that the slight risk of TSS associated with use of the Sponge did not warrant withdrawal of its approval. After reexamining the evidence concerning the Sponge and TSS, we continue to believe that the risk of Sponge users acquiring TSS is small, the warnings about TSS on the labeling of the Sponge appropriately address concerns about TSS, and withdrawal of approval of the Sponge is not warranted.

In March 2000, FDA's Division of Drug Risk Evaluation I performed a postmarketing safety review of the Sponge and identified 156 cases of possible TSS. Between 1983 and 1994, there were 89 cases that met at least 3 of the 5 CDC criteria for TSS diagnosis. Fourteen of the 89 had other possible contributing factors such as menstruation and/or possible tampon use within 7 days.¹⁸ In 85 percent of suspected TSS cases, the women used the Sponge for no more than 30 hours as instructed on the label. FDA's Adverse Event Reporting System records show a decline over time in the number of annual reported cases of suspected Sponge-associated TSS following initial marketing of the Sponge. In 1983 and 1984, there were a total of 35 cases where individuals met at least three of the five diagnostic criteria for TSS. In 1993 and 1994, seven such cases were reported. The literature suggests that there were approximately 1.5 million American women using the Sponge each year during the mid-1980s, making the actual occurrence of TSS quite low.¹⁹

The outer carton of the Sponge as labeled for reintroduction to the market contains the following warning statement concerning TSS:

¹⁷ Your earlier petitions in Docket No. 1983P-0187 were submitted on May 31, 1983, and February 27, 1992.

¹⁸ The label on the outer carton of the Sponge states: "Do not use during your menstrual period."

¹⁹ "The Sponge at Three Years: Research Studies New, Rehashes Old Questions," *Contraceptive Technology Update*, 7: 80-82, 1986.

Toxic Shock Syndrome: Some cases of Toxic Shock Syndrome (TSS) have been reported in women using barrier contraceptives, including the sponge. TSS is a rare, but serious disease that may cause death. Warning signs of TSS include fever, nausea, vomiting, diarrhea, muscle pain, dizziness, faintness, or a sunburn-like rash on face or body. If you have any of these signs, remove the sponge and get medical help right away.

The consumer information leaflet inside the carton contains the same warning, but ends with the following statement:

You can avoid the risk of getting sponge-associated TSS by not using the sponge.

In sum, FDA has concluded that the small risk of TSS associated with the use of the Sponge does not justify withdrawal of its approval. We believe the warnings in the labeling of the Sponge adequately advise consumers of this risk.

E. Adverse Events Underreporting

You state that Sponge users may not be aware of the tissue damage associated with use of the Sponge, so that consumer complaints represent only a small fraction of the women who may have experienced harm (Petition at 8-9). You also state that young people may not report complaints because of embarrassment and privacy concerns (Petition at 9).

We are aware that adverse events are underreported in general, and that adverse events associated with OTC products may be more underreported than those associated with prescription products. We agree that one possible cause of underreporting in this instance is that women may not have symptoms associated with vaginal irritation. We also note that there are many causes of intermittent asymptomatic vaginal inflammation aside from use of N-9 containing products. Such inflammation may occur because of tampon use, barrier contraceptive use, sexual intercourse, bacterial vaginosis, candida, and exposure to other agents like soaps, vaginal moisturizers, and douches. We believe, however, the label warnings and the consumer information leaflet for the Sponge adequately communicate that use may be associated with symptomatic or asymptomatic vaginal irritation that may increase the risk of acquiring HIV and other STDs from an infected partner. The Sponge also carries the warning that use of the Sponge does not protect against HIV or STDs and that use of a latex condom does protect against these infections. Therefore, your arguments concerning the potential underreporting of consumer complaints related to Sponge use do not alter our conclusion that approval of the Sponge should not be withdrawn.

F. Removing the Sponge

You state that removal problems are among the problems most commonly reported with the Sponge. "In the course of removing this product, prolonged exposure of the vagina to spermicide and additional vaginal damage may occur as a women [sic] attempts to probe her vagina to remove the Sponge" (Petition at 8).

We do not believe that the possibility of removal problems constitutes a valid reason for withdrawing approval of the Sponge. The current labeling for the Sponge contains detailed written and diagrammatic instructions for proper removal of the Sponge. In addition, the labeling provides instructions for removal when the Sponge is upside-down, torn, or seems to be stuck. A toll-free phone number is provided, and women are directed to a healthcare provider in situations where suggested maneuvers have not resulted in successful and complete Sponge removal. A woman is unlikely to cause injury by examining her vagina with her fingers to remove a vaginal contraceptive.

IV. Conclusion

For the reasons discussed above, your request that we remove the Sponge from the market is denied. The available evidence does not show that the Sponge is unsafe for use under the conditions of use for which it is approved or that it has not been shown to be safe under those conditions. Accordingly, we conclude that no grounds currently exist to justify withdrawal of approval of the Sponge.

Sincerely,



Steven K. Galson, M.D., M.P.H.
Acting Director
Center for Drug Evaluation and Research

Enclosure